OUTLINE OF THE PROPOSED WORK FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN PHARMACEUTICAL SCIENCES AND TECHNOLOGY

Submitted To

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Topic

"QUANTITATIVE DETERMINATION OF DRUGS IN BULK AND PHARMACEUTICAL DOSAGE FORM AND ITS VALIDATION USING HPLC"

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AIM & OBJECTIVE:

The primary objective of method development and validation in the analysis of the drug is to design and develop methods preferably instrumental one such as UV spectrometric, HPLC, GLC that are sensitive and reproducible when applied for analysis of marketed formulations.

In summary, the primary objective of proposed work is to:

- Develop new, simple, sensitive, accurate and economical analytical method for the determination of assay of the title ingredient by HPLC.
- Validate the proposed method in accordance with ICH guidelines for the intended analytical application, i.e. to apply the proposed method for analysis of the drugs in its dosage form.
- To perform the forced degradation studies indicating stable method.

INTRODUCTION:

HPLC is the most versatile and widely used type of elution chromatography. The technique is used to separate and determine species in a variety of organic, inorganic, and biological materials. HPLC is used either in the liquid-solid adsorption chromatography mode or the liquid-liquid partition chromatography mode, either normal or reversed-phase. Both partition and adsorption chromatography operates on differences in solute polarity. Polarity is important in determining both adsorption and solubility. As a general rule, highly polar materials are best separated using partition chromatography, while very non polar are separated using adsorption chromatography.

Method development and validation are essential parts of the pharmaceutical drug approval process. As process modifications are made and approval criteria become increasingly stringent, changes to the validated method are sometimes necessary. Many different approaches are applied to develop chromatographic methods today, including trial and error, method and column scouting, and software-based approaches such as first-principles approach and simplex optimization procedures. These approaches cannot, however, determine the effects of complex interactions between method variables or measure method robustness.

NEED OF STUDY

The number of drugs introduced into the market is increasing every year. These drugs may be either new entities or partial structural modification of the existing one. Very often there is a time delay from the date of introduction of a drug into the market to the date of its inclusion in pharmacopoeias. This happens because of the possible uncertainties in the continuous and wider usage of these drugs, reports of new toxicities (resulting in their withdrawal from the market), development of long-suffering opposition and introduction of better drugs by competitors. Under these conditions, standards and analytical procedures for these drugs may not be available in the pharmacopoeias. It becomes necessary, therefore to develop newer analytical methods for such drugs.

In 1987, US-FDA issued the guideline for submitting Documentation for the stability of Human drugs and Biologicals. In June 1998, FDA issued the draft guidance for stability testing of drug substances and products. The ICH guidelines which came into force from 6th Feb. 2003, require conduct of Forced Degradation studies under various conditions of pH, light, oxidation, dry heat etc. Review of literature reveals large number of methods reported over the period of last ten years, under the nomenclature of `Stability indicating' but many of them fall short of expectations of current regulatory requirements. Most of the methods report forced decomposition studies on the bulk drug only. Based on this observation, it is intend to carry out comparative evaluation of extent of degradation of bulk and its formulation. The study will include the drugs available singly and some drugs available in combination.

PLAN OF WORK:

Different phases of Research work planned are as follows:-

a) Literature survey

b) Selection of drug or drug combinations

c) Development of assay method

d) Preliminary Forced degradation studies of Bulk drug

e) Evaluation of `Stability – indicating' nature of assay method

f) Validation of assay method

g) Evaluation of stability samples by the developed `Stability – indicating' method

h) Accelerated stability testing of formulation

i) Comparison of different marketed samples if feasible

DURATION OF WORK:

Sr. No.	Work to be Completed	Duration
1	Review of Literature	4 Months
2	Procurement and selection of drug/drug combinations for the method development	2 Months
3	Development of chromatographic methods for selected drug candidates	8 Months
4	Development of stress degraded samples of individual drugs; confirming suitability of the methods developed above	8 Months
5	Validation of developed method as per ICH Guidelines	8 Months
6	Accelerated stability testing of formulation	6 Months
Total Duration of Project		**36 Months**

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